

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1(Original): A composition comprising a conjugate formed by

- (a) a modified metallothionein (MT) amino acid sequence or fragment thereof that binds the megalin receptor less avidly than naturally-occurring metallothionein; and
- (b) at least one or multiple molecules of a therapeutic divalent metal ion.

2 (Original): The composition according to claim 1, wherein said modified MT does not bind megalin.

3 (Original): The composition according to claim 1, wherein said modified MT comprises a modified β -MT subunit sequence
MDPNC₁SC₂ATGNSC₃TC₄ASSC₅KC₆KEC₇HC₈TSC₉X SEQ ID NO: 2, wherein X is any uncharged or negatively charged amino acid and is not K.

4 (Original): The composition according to claim 1, wherein said modified MT comprises a modified α -MT subunit sequence
X'SC₁₀C₁₁SC₁₂C₁₃PAGC₁₄TKC₁₅AQGC₁₆IC₁₇KGASDKC₁₈SC₁₉C₂₀A, SEQ ID NO: 3, wherein X' is any uncharged or negatively charged amino acid and is not K.

5 (Currently amended): The composition according to claim 1, wherein said modified MT comprises a modified MT sequence
MDPNC₁SC₂ATGNSC₃TC₄ASSC₅KC₆KEC₇KC₈TSC₉X X'SC₁₀C₁₁SC₁₂C₁₃PAGC₁₄

TKC₁₅AQGC₁₆IC₁₇KGASDKC₁₈SC₁₉C₂₀A, SEQ ID NO: 4, wherein X and X' are independently selected from any uncharged or negatively charged amino acid and ~~[[is]]~~are not K.

6 (Currently amended): The composition according to ~~any of claims 3 to 5~~claim 3, wherein all C residues in said sequence are invariant.

7 (Currently amended): The composition according to ~~claim 3 and 5~~claim 3, wherein said modified MT is truncated at the amino or carboxy terminus.

8 (Currently amended): The composition according to ~~any claims 3 to 5~~claim 3, wherein X or X' is Q.

9 (Currently amended): The composition according to ~~any of claims 3 to 5~~claim 3, wherein any amino acid other than C is modified by substitution with a non-naturally-occurring amino acid.

10 (Currently amended): The composition according to ~~any of claims 3 to 5~~claim 3, wherein said modified MT comprises a fusion protein comprising multiple copies of full-length MT or subunit fragments thereof, wherein the fusion protein has an overall negative or neutral charge or a negative or neutral charge at the positions indicated by X and X'.

11 (Original): The composition according to claim 1, wherein said conjugate has size greater than 70 kD.

12 (Original): The composition according to claim 1, wherein the number of molecules of heavy metals complexes to a single modified MT or fragment thereof range from 1 to 7.

13 (Original): The composition according to claim 1, wherein said divalent metal ions are selected from the group consisting of anti-neoplastic platinum compounds, cadmium, and copper.

14 (Original): The composition according to claim 1, wherein said conjugate further comprises

(c) a delivery peptide for targeted delivery to a desired cell, wherein said delivery peptide is fused to said modified MT or fragment thereof.

15 (Original): The composition according to claim 1, further comprising a pharmaceutically acceptable carrier.

16 (Original): The composition according to claim 1, further comprising a second therapeutic compound or composition.

17 (Original): A method for treating cancer comprising administering to a mammalian subject an effective amount of the composition of claim 1, wherein said treatment inhibits the renal uptake of said divalent metal ions.

18 (Canceled).

19 (Original): A method for inhibiting renal uptake of therapeutic divalent metals ions comprising administering said ions as part of a conjugate of a composition of claim 1.

20 (Original): A metallothionein derivative amino acid sequence that does not bind megalin as avidly as naturally occurring metallothionein.